Free Water Extraction from Diffusion Images

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Introduction In diffusion imaging of the brain one often encounters voxels which contain a mixture of brain tissue with free water. Usually this occurs next to the ventricles (CSF contamination), but it could also appear when edema occupies a space sheared with brain tissue. As a result diffusion properties of the tissue are occluded by the diffusion properties of free water and will be miscalculated with traditional analysis such as DTI. By modeling the diffusion with a free water compartment in addition to a separate tissue compartment we are able both to assess the diffusion properties of the tissue, and at the same time map the amount of free water. In order to do so we rely on a mathematical framework that stabilizes the fitting of the model by adding physical and biological constraints. With this framework we can answer the question "what is the best amount of free water which upon removal leaves the most 'biological' tissue compartment?" We explain the principles of the framework, and present free water maps obtained for a healthy subject and for a patient suffering from edema (surrounding a tumor). We also show the effect of eliminating the free water compartment by comparing FA and tractography obtained for the tissue compartment, relative to the same analysis preformed by conventional DTI on the entire voxel.

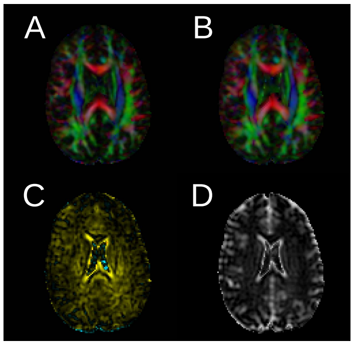

Fig 1: **CSF contamination.** Applying free water extraction enhances FA of fibers especially next to the ventricles. The DTI color-code (a) is very similar to the tissue compartment color-code (b), yet a FA differences map (c) shows that FA had been increased where partial volume had been found. The free water map (d) portraits the voxels found to have partial volume, and delineates the CSF-brain tissue interface.

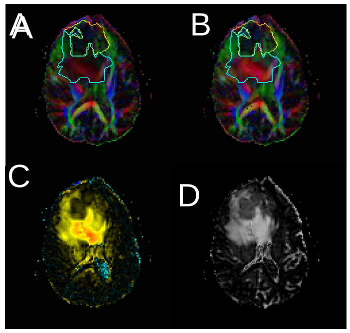

Fig 2**: Edema.** DTI color coded map (a) shows low FA in the area of the edema (cyan) and tumor (yellow). After extracting free water we get enhanced FA within the edema (b), where the Corpus Callosum is expected to pass. The FA differences image (c) demonstrates that the effect is limited to the edema, and around the ventricles. The extracted free water map (d) delineates the edema.

Theory Most attempts in the literature to avoid CSF contamination are by water suppressing sequences such as FLAIR. The use of modeling for the problem was first proposed by Pierpaoli and Jones *[1]*, based on the bi-tensor model *[2]*. This approach was further investigated in *[3]*. The bi-tensor model fits the data with two components: one restricted to have free water diffusivities (isotropic tensor with eigenvalues of free water), and the other is modeled by a diffusion tensor parameter. The volume fraction between components is controlled by an additional parameter. The inverse problem of fitting this model (i.e., finding the two parameters) to diffusion attenuation signal is ill-posed. This is since for any chosen volume fraction of water compartment there could be found a tensor to fit the remaining signal. The fitting problem was avoided in *[1]* by using a number of b-weightings, which allows a bi-exponential fit. Our approach reduces the minimal acquisition required to a single b-value DTI sequence (which is nowadays available with most commercial scanners), by stabilizing the problem with a variational regularization framework. We use the *Beltrami regularization with Iwasawa Coordinates* (BRIC) framework *[4]* which is a fast converging minimization process that incorporates physical and biological constraints to iteratively fit the bi-tensor model. Physical constraints restrict the volume fraction parameter per voxel: for any selected value we can calculate what would have been the attenuation signal for each applied gradient, had the voxel contained only the tissue compartment. This attenuation has to be in the range [0,1], thus restricting a minimal tissue volume fraction, and reducing the search space. Biological constraints restrict tensor variations: as with any biological or physical measurement, we assume that the values obtained have to be piece-wise smooth. This means that once the water compartment had been removed, we expect in neighboring voxels to have similar tensor values (with a gradual change), unless they are exactly on a contour line that separates between tissue types. Piece-wise smooth tensor variation is achieved by the Beltrami operator. As a result we obtain a volume fraction parameter for each voxel, and a piece-wise smooth tensor field to describe the tissue compartment, had it been the only compartment imaged.

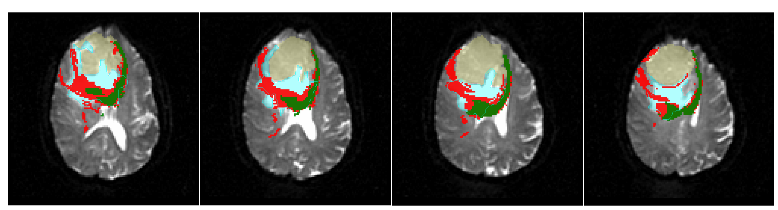

Fig 3: **Tractography**. After free water extraction the fibers (red) were able to delineate the corpus callosum. The original tracts (green, overlaid on top) had been terminated at the edema. Presented are four consecutive axial slices for the data shown at Fig 2 (tumor marked by yellow and the edema marked by

Results and Discussion We demonstrate the free water extraction on a healthy volunteer dataset (GE 3T, 48 slices, 1.5mm X 1.5 mm in plane resolution, 3 mm slice thickness, TR=12sec, TE=76.5ms, 19 gradient directions, b=1000 and NEX=1), and on a clinical dataset of a patient suffering from massive edema surrounding a tumor (GE 1.5T, 24 slices, 1.8mm X 1.8 mm in plane resolution, 6 mm slice thickness, TR=10sec, TE=98ms, 6 gradient directions, b=1000 and NEX=4). For the healthy patient the effect of free water removal is mainly where CSF contamination occurs, for fibers that pass next to the ventricles (Fig 1). The remaining of the data appears unaffected. On the clinical dataset, tracking the fiber through the edema was not possible with DTI, due to low FA (Fig 2). Tractography was initiated at the left side of the brain which was not contaminated with edema, and without free water elimination all tracts were stopped within the edema (Fig 3, green colored tracts stopping at the cyan colored edema). The edema removal procedure reveals the missing tract, and is able to track through the edema (Fig 3, red colored tracts). This suggests that at the time of the scan the corpus callosum had some cross-hemisphere connectivity. The assessed free water map (Fig 2D) can be used for better evaluation of the intensity and location of the edema.

Summary We have demonstrated the importance of free water extraction in the process of inferring diffusion properties of brain tissue. While the effect of free water elimination for healthy subjects is mainly restricted to the white matter – CSF interface, it can no longer be neglected when dealing with other "free water" induced artifacts such as edema. The strength of our method is in its clinical relevance, we allow a conventional DTI acquisition, and are able to extract the missing information by using neighborhood alignment and a priori physical constraints.

References:*[1]* Pierpaoli and Jones, ISMRM, 2004; 12:1215. *[2]* Alexander et al., MRM 48, 2002. *[3]* Pasternak et al. NIPS 2005:704 *[4]* Gur et al. MMBIA 2007.